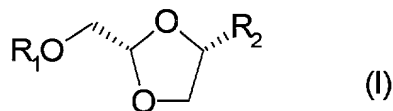


5 CLAIMS:

1. A method of treating a patient having a cancer comprising administering to said patient a compound having the following formula:

10



wherein:

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R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof, wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

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25

R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₁₈ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxycarbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl; saleginyl, t-butyl, phosphate or diphosphate;

30

R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

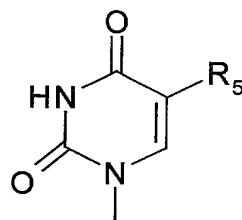
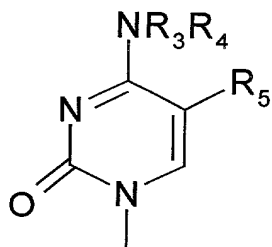
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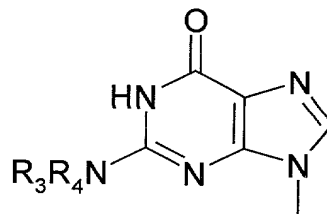
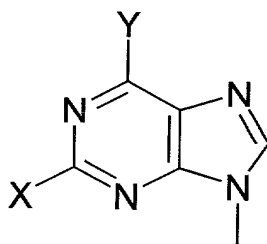
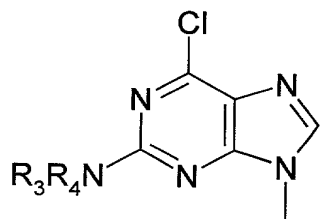
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R_2 is

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R_3 and R_4 are in each case independently H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-18} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

30

R_6 is, in each case, H, C_{1-20} alkyl, C_{2-20} alkenyl, C_{0-20} alkyl- C_{6-24} aryl, C_{0-20} alkyl- C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S; and

35

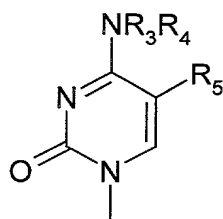
R_7 is, in each case, C_{1-20} alkyl, C_{2-20} alkenyl, C_{6-10} aryl, C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, $-C(O)R_6$, $-C(O)OR_6$, and

40

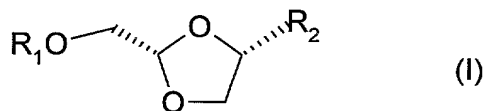
X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

2. A method according to claim 1, wherein at that least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆, -C(O)OR₆ or -C(O)NHR₆, then R₆ is other than H.

3. A method according to claim 1, wherein R₂ is of the formula:



4. A method of treating a patient with cancer, wherein the cancer cells are deficient in nucleoside or nucleobase transporter proteins, comprising administering to said patient a compound according to the following formula:



wherein:

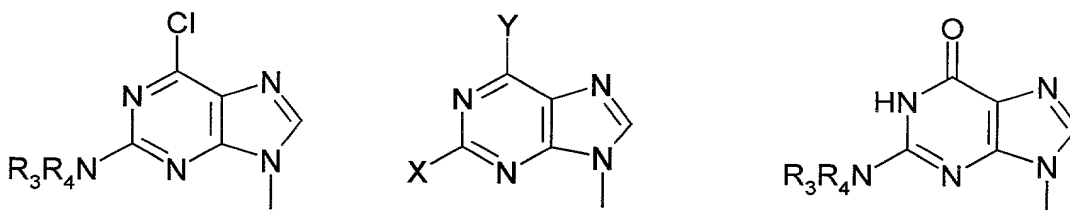
R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic

thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-18} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxycarbonyloxymethyl, or C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate or triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-18} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn

5 and Gln, and which in each case is optionally terminated by -R₇;

R₆ is, in each case, H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₁₈ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally
10 containing 1-3 heteroatoms selected from the group comprising O, N or S;

R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms
15 selected

from the group comprising O, N or S, -C(O)R₆,
-C(O)OR₆, and

X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or
20 a pharmaceutically acceptable salt thereof.

5. A method according to claim 4, wherein at least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆, -C(O)OR₆, or -C(O)NHR₆ then R₆ is other
25 than H.

6. A method according to claim 4, wherein said cancer cells are deficient in one or more nucleoside or nucleobase transporter proteins that provide sodium-independent,
30 bidirectional equilibrative transport.

7. A method according to claim 4, wherein said cancer cells are deficient in nucleoside or nucleobase transporter proteins that provide sodium-dependent, inwardly directed
35 concentrative processes.

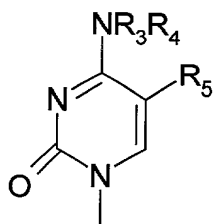
8. A method according to claim 7, wherein said cancer cells are deficient in nucleoside or nucleobase transporter proteins that provide sodium-dependent, inwardly directed
40 concentrative processes.

5 9. A method according to claim 4, wherein said cancer cells are deficient in es transporter proteins, ei transporter proteins or both.

10 10. A method according to claim 4, wherein said cancer cells are deficient in cit transporter proteins, cib transporter proteins, cif transporter proteins, csg transporter proteins, cs transporter proteins, or combinations thereof.

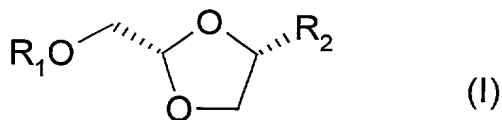
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11. A method according to claim 4, wherein R_2 is of the formula:



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25 12. A method of treating patients with cancer comprising administering to said patient a compound of the following formula:



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wherein:

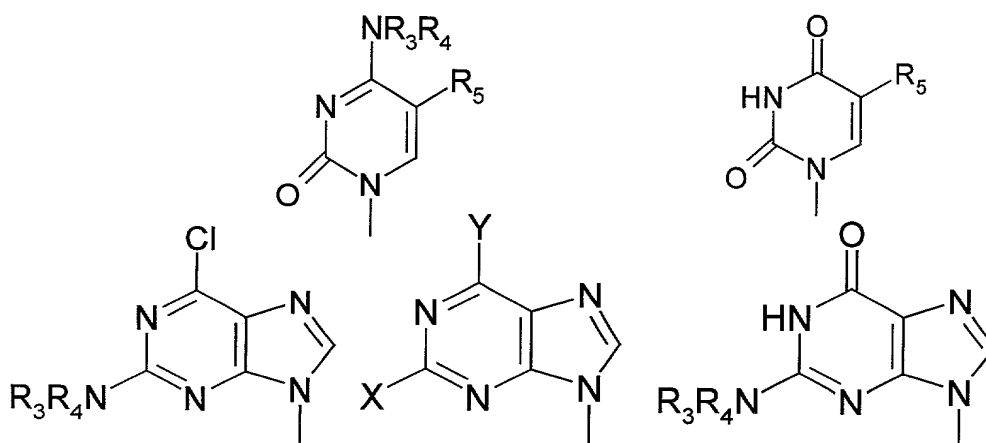
35 R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-20} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gly, and which in each case is optionally terminated by $-R_7$;

40

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-18} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxy carbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-20} alkyl; C_{2-20} alkenyl; C_{6-10} aryl; C_{5-10} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile,

Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and at least one amino acid is not Gly, and which in each case is optionally terminated by $-R_7$;

R_6 is, in each case, H, C_{1-20} alkyl, C_{2-20} alkenyl, C_0 -

alkyl- C_{6-10} aryl, C_{0-20} alkyl- C_{5-10} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing

1-3 heteroatoms selected from the group comprising O, N or S;

R_7 is, in each case, C_{1-20} alkyl, C_{2-20} alkenyl, C_{6-10} aryl, C_{5-10} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected

from the group comprising O, N or S, $-C(O)R_6$, $-C(O)OR_6$, and

X and Y are each independently Br, Cl, I, F, OH, OR_3 or NR_3R_4 and at least one of X and Y is NR_3R_4 ;

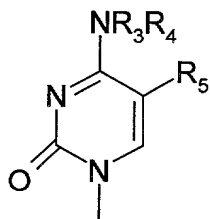
with the proviso that least one of R_1 , R_3 and R_4 is other than H, and if R_3 and R_4 are both H and R_1 is $-C(O)R_6$, $-C(O)OR_6$, or $-C(O)NHR_6$ then R_6 is other than H; or

a pharmaceutically acceptable salt thereof;

wherein said compound is administered at least daily

for a period of 2 to 10 days.

13. A method according to claim 12, wherein R_2 is of the formula:



14. A method of treating a patient with cancer wherein the cancer is resistant to cytarabine, said method

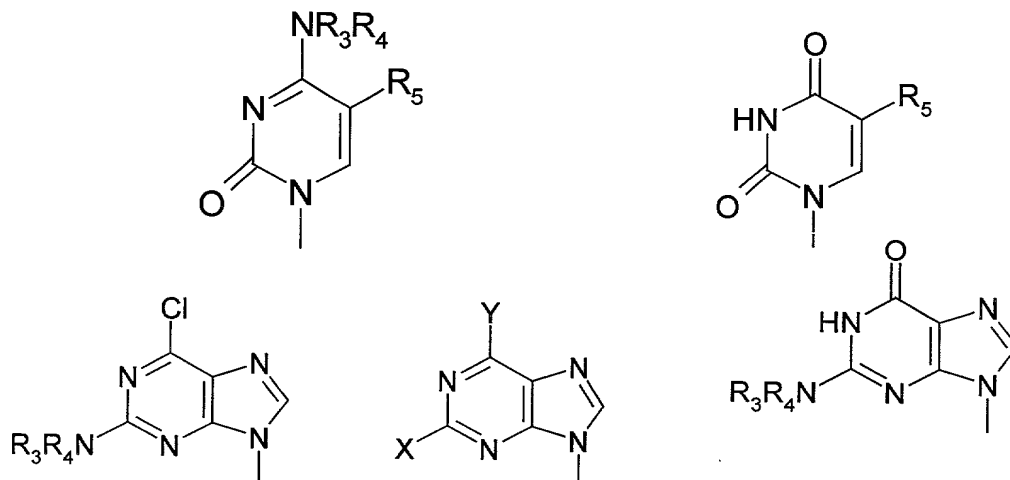
comprising administering to said patient a compound according to the following formula:

R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-20} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NRH_6$; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-18} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxy carbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-18}

heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or a tripeptide chain or mimetic thereof wherein the amino acids are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

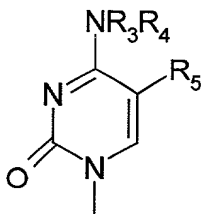
R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₂₄ heteroaromatic ring, C₃₋₂₄ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

R₇ is, in each case, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₅₋₂₄ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆; and

X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

15. A method according to claim 14, wherein at least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆; -C(O)OR₆, or -C(O)NHR₆ then R₆ is other than H.

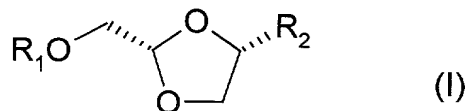
16. A method according to claim 14, wherein R₂ is of the formula:



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17. A method of treating a patient with cancer comprising:

determining that a compound enters cancer cells predominately by passive diffusion; and administering said compound to said patient; wherein said compound is a compound according to the formula:



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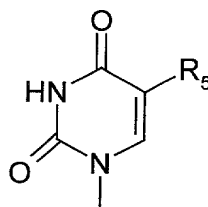
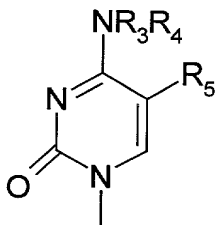
wherein:

R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-24} heteroaromatic ring; C_{3-24} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-\text{C}(\text{O})\text{R}_6$; $-\text{C}(\text{O})\text{OR}_6$; $-\text{C}(\text{O})\text{NHR}_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-\text{R}_7$;

R_1 can also be a $\text{P}(\text{O})(\text{OR}')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-24} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxycarbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

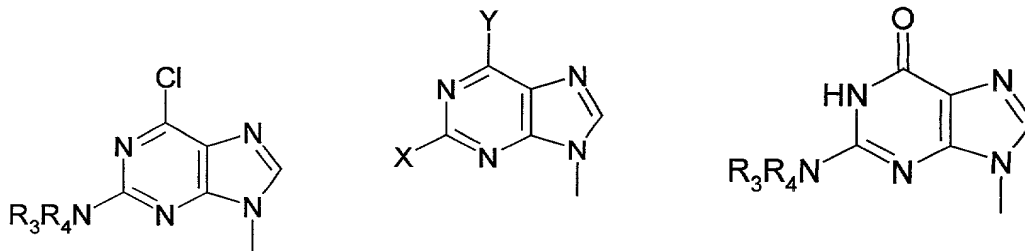
R_2 is



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R_3 and R_4 are in each case independently H; C_{2-24} alkyl; C_{1-24} alkenyl; C_{6-24} aryl; C_{5-24} heteroaromatic ring; C_{3-24} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_6 is, in each case, H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{0-20} alkyl- C_{6-24} aryl, C_{0-20} alkyl- C_{5-24} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

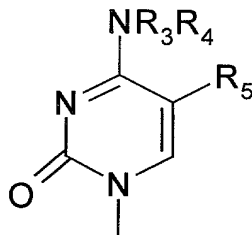
R_7 is, in each case, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{5-24} heteroaromatic ring, C_{3-20} nonaromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, $-C(O)R_6$, $-C(O)OR_6$, and

X and Y are each independently Br, Cl, I, F, OH, OR_3 or NR_3R_4 and at least one of X and Y is NR_3R_4 ; or a pharmaceutically acceptable salt thereof.

18. A method according to claim 17, wherein at least one of R_1 , R_3 and R_4 is other than H, and if R_3 and R_4 are both H and R_1 is $-C(O)R_6$ or $-C(O)OR_6$, then R_6 is other than H.

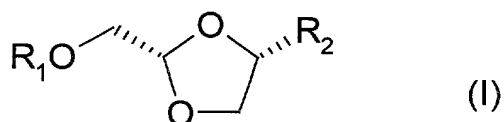
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19. A method according to claim 17, wherein R_2 is of the formula:



20. A method of treating a patient with cancer comprising:

- administering to said patient a compound which has been determined to enter the cancer cells predominately by passive diffusion, wherein said compound is a compound according to the formula:



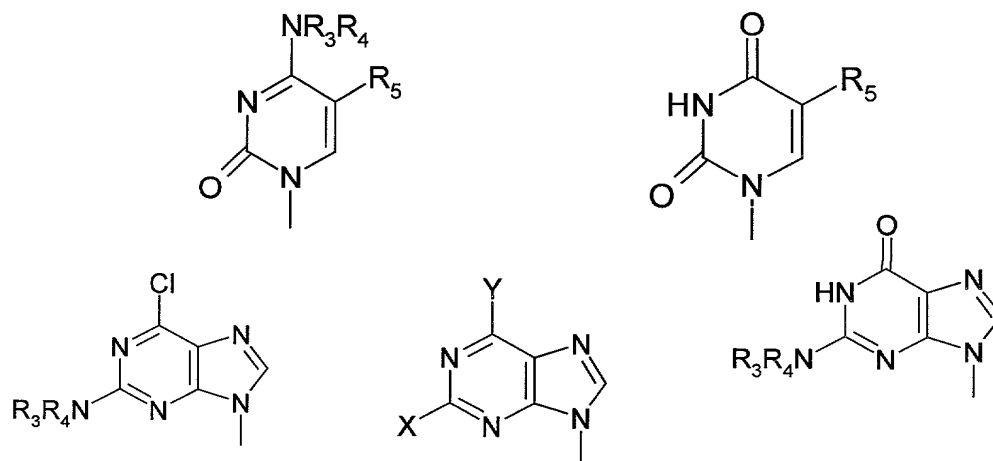
wherein:

R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-24} heteroaromatic ring; C_{3-24} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-18} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxycarbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-24} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_6 is, in each case, H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{0-20} alkyl- C_{6-24} aryl, C_{0-20} alkyl- C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

R_7 is, in each case, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms

5 selected from the group comprising O, N or S,
 $-C(O)R_6$, $-C(O)OR_6$, and

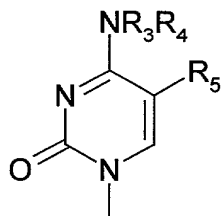
X and Y are each independently Br, Cl, I, F, OH, OR_3
 or NR_3R_4 and at least one of X and Y is NR_3R_4 ; or a
 pharmaceutically acceptable salt thereof.

10

21. A method according to claim 20, wherein at least one
 of R_1 , R_3 and R_4 is other than H, and if R_3 and R_4 are both
 H and R_1 is $-C(O)R_6$; $-C(O)OR_6$ or $-C(O)NHR_6$ then R_6 is other
 than H.

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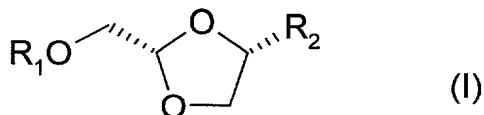
22. A method according to claim 20, wherein R_2 is of the
 formula:



25

30 23. A method of treating a patient with cancer resistant
 to troxacitabine, comprising administering to said patient
 a troxacitabine derivative having a greater lipophilicity
 than troxacitabine.

35 24. A method according to claim 23, wherein said
 derivative is a compound of the following formula:



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wherein:

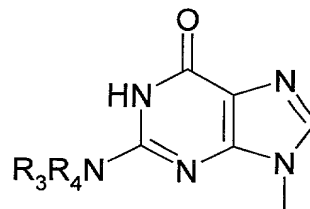
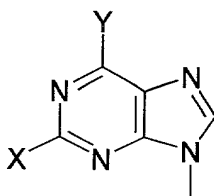
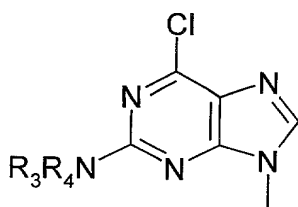
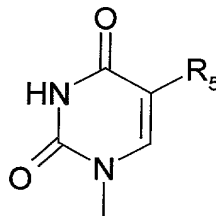
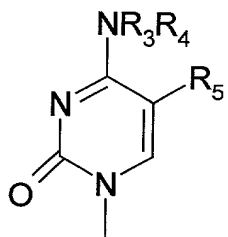
45 R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-24}
 heteroaromatic ring; C_{3-20} non-aromatic ring
 optionally containing 1-3 heteroatoms selected
 from the group comprising O, N, or S; $-C(O)R_6$;
 $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or

dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln and the amino acid chain contains at least one amino acid other than Gly, and which in each case is optionally terminated by $-R_7$;

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-24} arylmethyl, C_{2-17} acyloxymethyl, C_{3-8} alkoxycarbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-20} alkyl; C_{2-20} alkenyl; C_{6-10} aryl; C_{5-10} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms

selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln and the amino acid chain contains at least one amino acid other than Gly, and which in each case is optionally terminated by $-R_7$;

R_6 is, in each case, H, C_{1-20} alkyl, C_{2-20} alkenyl, C_{0-20} alkyl- C_{6-10} aryl, C_{0-20} alkyl- C_{5-10} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

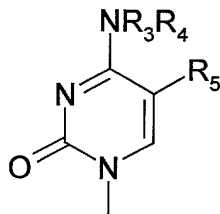
R_7 is, in each case, C_{1-20} alkyl, C_{2-20} alkenyl, C_{6-10} aryl, C_{5-10} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, $-C(O)R_6$, $-C(O)OR_6$, and

X and Y are each independently Br, Cl, I, F, OH, OR_3 or NR_3R_4 and at least one of X and Y is NR_3R_4 ;

with the proviso that least one of R_1 , R_3 and R_4 is other than H, and if R_3 and R_4 are both H and R_1 is $-C(O)R_6$, $-C(O)OR_6$ or $-C(O)NHR_6$, then R_6 is other than H; or

a pharmaceutically acceptable salt thereof.

25. A method according to claim 24, wherein R_2 is of the formula:

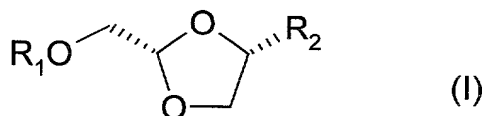


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26. A method of treating a patient with cancer comprising:

determining that a compound does not enter cancer cells predominately by nucleoside or nucleobase transporter proteins; and administering said compound to said patient; wherein said compound is a compound according to the formula:

10



15

wherein:

R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

20

25

R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₂₄ arylmethyl, C₂₋₁₇ acyloxymethyl, C₃₋₈ alkoxycarbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

30

35

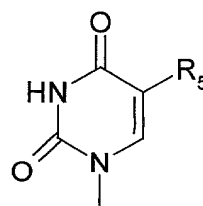
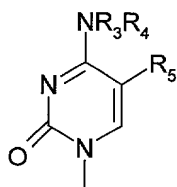
R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

40

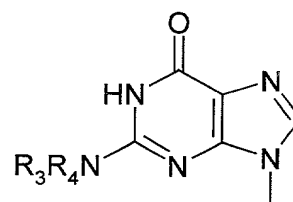
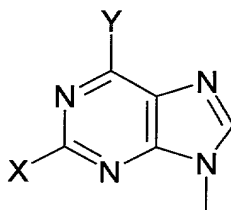
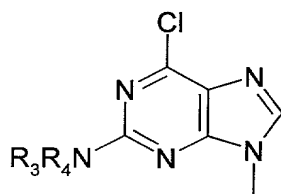
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R_2 is

10



15



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R_3 and R_4 are in each case independently H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-24} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

30

35

R_6 is, in each case, H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{0-20} alkyl- C_{6-24} aryl, C_{0-20} alkyl- C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

40

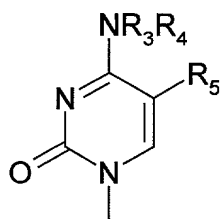
R_7 is, in each case, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{5-20} heteroaromatic ring, C_{3-20} non-aromatic

5 ring optionally containing 1-3 heteroatoms
selected from the group comprising O, N or S,
-C(O)R₆, -C(O)OR₆, and

X and Y are each independently Br, Cl, I, F, OH, OR₃
or NR₃R₄ and at least one of X and Y is NR₃R₄; or a
10 pharmaceutically acceptable salt thereof.

27. A method according to claim 26, wherein at least one
of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both
H and R₁ is -C(O)R₆, -C(O)OR₆ or -C(O)NHR₆ then R₆ is other
15 than H.

28. A method according to claim 27, wherein R₂ is of the
formula:



29. A method according to any one of claims 1-28, wherein
said cancer is prostate cancer, colon cancer, lung
cancer, melanoma, ovarian cancer, renal cancer,
breast cancer, lymphoma, pancreatic cancer or bladder
cancer.

30. A method according to any one of claims 3-28, wherein
said cancer is leukemia.

31. A method according to any one of claims 1-28, wherein
at least one of R₁, R₃, or R₄ is piperazinyl,
piperidinyl, morpholinyl, pyrrolidinyl, adamantyl or
quinuclidinyl.

32. A method according to any one of claims 1-28, wherein
at least one of R₁, R₃ or R₄ is acetyl, propionyl, butyryl,
valeryl, caprioic, caprylic, capric, lauric, myristic,
palmitic, stearic, oleic, linoleic, or linolenic.

5 33. A method according to any one of claims 1-28, wherein at least one of R_1 , R_3 or R_4 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl or biphenyl.

10 34. A method according to any one of claims 1-28, wherein at least one of R_1 , R_3 or R_4 contains a heterocyclic group selected from the following group:

furyl, thiophenyl, pyrrolyl, imidazolyl, pyrazoyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadrazolyl, 15 thiadiazolyl, thiopyranyl, pyrazinyl, benzofuryl, benzothiophenyl, indolyl, benzimidazolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiozolyl, benzisothiazolyl, benzoxadiazolyl, quinolinyl, isoquinolinyl, carbazolyl, acridinyl, cinnolinyl and 20 quinazolinyl.

35. A method according to any one of claims 1-28, wherein said compound is administered at least daily for a period of 2 to 10 days every 2 to 5 weeks.

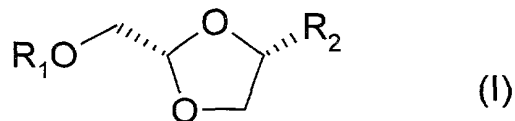
25 36. A method according to any one of claims 1-28, wherein said compound is administered at least daily for a period of 2 to 10 days every 3 to 4 weeks.

30 37. A method according to any one of claims 1-28, wherein said compound is administered at least daily for 3 to 7 days every 2 to 5 weeks.

35 38. A method according to any one of claims 1-28, wherein said compound is administered at least daily 4 to 6 days every 2 to 5 weeks.

39. A compound having the following formula:

40



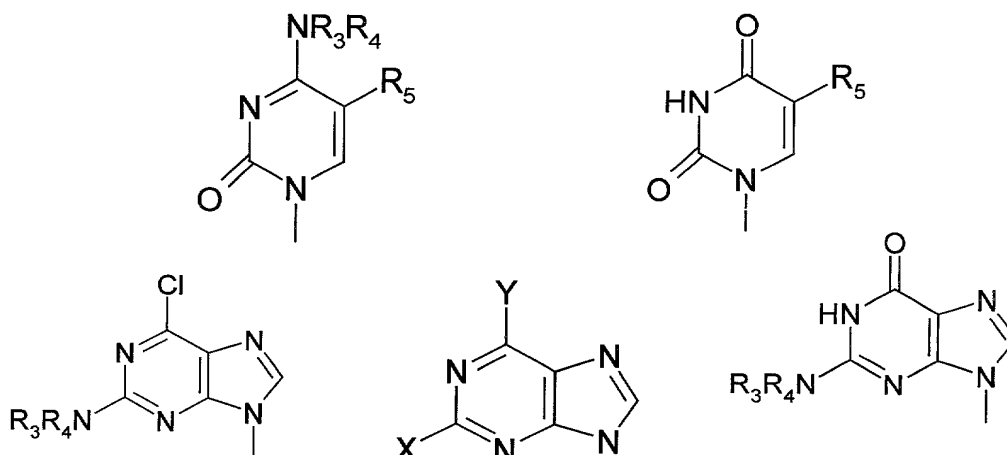
5 wherein:

R_1 is H; C_{1-20} alkyl; C_{2-20} alkenyl; C_{6-10} aryl; C_{5-10} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NRH_6$; or an amino acid radical or dipeptide or tripeptide chain wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Met, Cys, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-20} alkyl, C_{2-20} alkenyl, C_{6-10} aryl, C_{7-11} arylmethyl, C_{2-7} acyloxymethyl, C_{3-8} alkoxy carbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R_2 is



R_3 and R_4 are in each case independently H; C_{1-20} alkyl; C_{2-20} alkenyl; C_{6-10} aryl; C_{5-10} heteroaromatic ring; C_{3-20} non-aromatic ring

- 5 optionally containing 1-3 heteroatoms
selected from the group comprising O, N, or
S; -C(O)R₆; -C(O)OR₆; -C(O)NRH₆; or an amino
acid radical or dipeptide or tripeptide
chain or mimetic thereof wherein the amino
10 acid radicals are selected from the group
comprising Glu, Gly, Ala, Val, Leu, Ile,
Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn
and Gln, and which in each case is
optionally terminated by -R₇;
- 15 R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋₂₀
alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic
ring, C₃₋₂₀ non-aromatic ring optionally
containing 1-3 heteroatoms selected from the
group comprising O, N or S;
- 20 R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀
aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ nonaromatic
ring optionally containing 1-3 heteroatoms
selected from the group comprising O, N or S,
-C(O)R₆, -C(O)OR₆; and
- 25 X and Y are each independently Br, Cl, I, F, OH, OR₃
or NR₃R₄ and at least one of X and Y is NR₃R₄; or
a pharmaceutically acceptable salt thereof;
with the proviso that at least one of R₁, R₃ and
R₄ is
- 30 C₇₋₂₀ alkyl;
C₇₋₂₀ alkenyl;
C₆₋₁₀ aryl;
C₅₋₁₀ heteroaromatic ring;
C₄₋₂₀ non-aromatic ring optionally containing 1-3
- 35 heteroatoms selected from the group comprising O, N, or S;
C(O)R₆ in which R₆ is, C₇₋₂₀ alkyl, C₇₋₂₀ alkenyl,
C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring,
C₄₋₂₀ non-aromatic ring optionally containing 1-3
heteroatoms selected from the group comprising O, N or S;
- 40 -C(O)OR₆ in which R₆ is C₇₋₂₀ alkyl, C₇₋₂₀ alkenyl,
C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring,
C₄₋₂₀ non-aromatic ring optionally containing 1-3

5 heteroatoms selected from the group comprising O, N or S;
or

10 a dipeptide or tripeptide or mimetic thereof
where the amino acid radicals are selected from the
group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro,
Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and
which is optionally terminated by -R₇.

15 40. A method of treating a patient with cancer comprising
administering to said patient a prodrug form of
troxacitabine, having a lipophilic structure to enhance
entry of the prodrug into the cancer cells by passive
diffusion, wherein said lipophilic structure is cleavable
20 by cellular enzymes, thereby increasing the amount of
troxacitabine within the cancer cells to a level greater
than that allowable by administration of troxacitabine in
nonprodrug form.

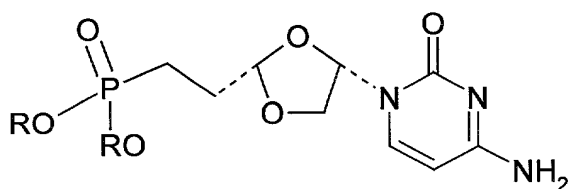
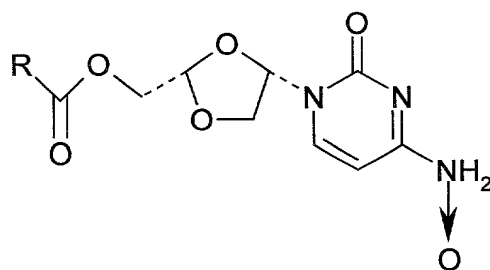
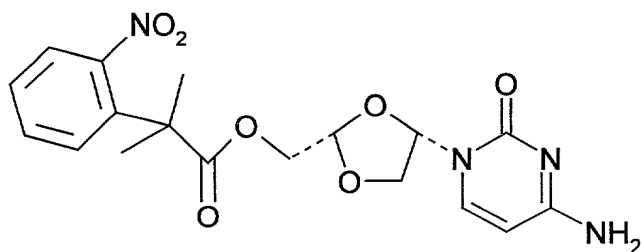
25 41. A method of treating a patient having cancer which is
resistant to gemcitabine, cytarabine or both, comprising
administering to said patient a troxacitabine derivative
having a lipophilic structure which enhances the entry of
the derivative into the cancer cell by the passive
diffusion.

30 42. A method of treating a patient having cancer wherein
the cancer cells are deficient in nucleoside or nucleobase
transporter proteins, comprising administering to said
patient a troxacitabine derivative having a lipophilic
structure which enhances entry of the derivative into the
35 cancer cells by passive diffusion.

40 43. A method according to claim 4, wherein said cancer
cells are deficient in one or more nucleobase transporter
proteins.

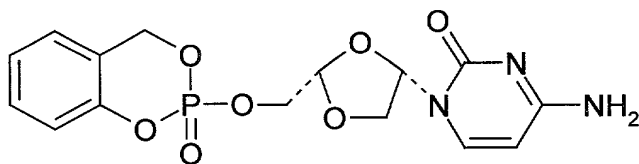
44. A method according to any one of claims 1-28, wherein
the compound is of the formulas

5



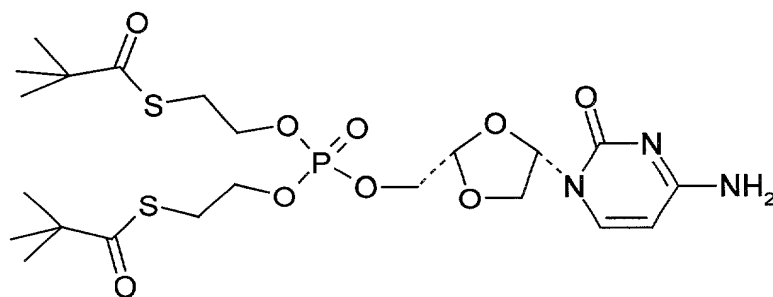
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45. A method according to any one of claims 1 to 28 wherein the compound is of the formula



15

46. A method according to any one of claims 1 to 28, wherein the compound is of the formula



- 5 46. A method according to any one of claims 1 to 28,
wherein the compound is selected from

4-HEXYL-BENZOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-
YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 191) ;

10 8-PHENYL-OCTANOIC ACID [1-(2-HYDROXYMETHYL-
[1,3]DIOXOLAN-4-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-
YL]-AMIDE (No. 197) ;

8-PHENYL-OCTANOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-
1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 198) ;

15 4-PENTYL-BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACID 4-(4-
AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-
YLMETHYL ESTER (No. 211) ;

4-PENTYL-CYCLOHEXANECARBOXYLIC ACID 4-(4-AMINO-2-OXO-
2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER
(No. 240) or mixtures thereof.

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